

## Title: METHODS OF MAKING HYBRID PROTEINS

Inventor: Peter B. Vander Horn - Filed: Herewith

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Figure 1 BLOSUM62 Substitution Matrix

	C	S	T	P	A	G	N	D	E	Q	H	R	K	M	I	L	V	F	Y	W
C	9	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
S	1	1	3		3	3	3	4	3	3	3	3	3	1	1	1	1	2	2	
T	-	1	4	1	-	1	0	1	0	0	0	-	0	-	-	-	-	-	-	
P	1		1	1	-	-	-	-	-	-	-	1	1	2	2	2	2	2	3	
A	3	1	7	-	-	1	2	1	1	1	2	2	1	2	3	3	2	4	3	
G	0	1	-	-	4	0	-	-	-	-	-	-	-	-	-	-	-	-	-	
N	1	0	-	-	0	6	1	0	0	-	0	0	-	-	-	0	-	3	3	
D	3	2		2	2	2	1	2	2	2	2	2	2	3	4	4	3	3	2	
E	0	1	-	-	-	1	6	2	0	-	1	2	1	3	3	4	3	3	4	
Q	4	1	2		0	2	5	2	0	0	1	-	-	-	-	-	-	-	-	
H	3	1	0	-	-	1	1	0	0	8	0	-	1	2	3	3	2	1	2	
R	1	2	1	2	1	2	2		0	1	0	5	2	-	-	-	-	-	-	
K	3	1	1	2	1	2	1		1	1	-	2	5	-	-	-	-	-	-	
M	1	1	1	2	1	3	2	3	2	0	-	2	1	5	1	2	-	0	-	
I	2	2	2	3	1	4	3	3	3	3	3	3	3	1	4	2	1	0	-	
L	1	2	2	3	1	4	3	4	3	2	3	2	2	2	2	4	3	0	-	
V	1	2	2	2	0	-	-	-	-	-	-	-	-	1	3	1	4	-	-	
F	2	2	2	4	2	3	3	3	3	3	1	3	3	0	0	0	-	6	3	
Y	2	2	2	3	2	3	2	3	2	1	-	2	2	1	1	1	1	3	7	
W	2	3	3	4	3	2	4	4	3	2	2	3	3	1	3	2	3	1	2	

Figure 2. Blast alignment of Pfu (query 1) against Deep Vent (subject 1)

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>qi|2494186|sp|Q51334|DPOL_PYRSD DNA polymerase (Deep Vent DNA polymerase)
[Contains: Endonuclease
 PI-PspI (Psp-GDB pol intein)]
Length = 1312

Score = 816 bits (2109), Expect = 0.0
Identities = 414/493 (83%), Positives = 459/493 (92%)

Query: 1 MILDVDYITEEGKPVIRLFKKENGKFKIEHDRTFRPYIYALLRDDS KIEEVKKITGERHG 60
        MILD DYITE+GKP+IR+FKENG+FK+E+DR FRPYIYALL+DDS+I+EV+KIT ERHG
Sbjct: 1 MILDADYITEDGKPIIRIFKENGFEKVEYDRNFRPYIYALLKDDSQIDEVRKITAERHG 60

Query: 61 KIVRIVDVEKVEKKFLGKPITVWKLYLEHPQDVPTIREKVREHPAVVDIFEYDIPFAKRY 120
        KIVRI+D EKV KKFLG+PI VW+LY EHPQDVPIR+K+REH AV+DIFEYDIPFAKRY
Sbjct: 61 KIVRIIDAEEKVKKFLGRPIEVWRFLYFEHPQDVPAIRDKIREHSAVIDIFEYDIPFAKRY 120

Query: 121 LIDKGLIPMEGEEELKILAFDIETLYHEGEEFGKGPIMISYADENEAKVITWKNIDL PY 180
        LIDKGLIPMEG+EELK+LAFDIETLYHEGEEF KGPIIMISYADE EAKVITWK IDLPY
Sbjct: 121 LIDKGLIPMEGDEELKLLAFDIETLYHEGEEFAKGPIIMISYADEEEAKVITWKKIDL PY 180

Query: 181 VEVVSSEREMIKRFLRIIREKD PDI IITYNGDSFD PLY KRAEKLGIKL TIGRDGSEPK 240
        VEVVSSEREMIKRFL++IREKDPD+I+TYNGDSFD PYL KRAEKLGIKL +GRDGSEPK
Sbjct: 181 VEVVSSEREMIKRFLKVI REKD PDI IITYNGDSFD PLY LVKRAEKLGIKL PLGRDGSEPK 240

Query: 241 MQRIGDMTAVEVKGRHIHF DLYHVITRTINLPTYTLEAVYEAI FGKPKEK VYADEIAK AWE 300
        MQR+GDMTAVE+KGRHIHF DLYHV RI TINLPTYTLEAVYEAI FGKPKEK VY A EIA+AWE
Sbjct: 241 MQRLGDMTAVEIKGRHIHF DLYHVIRRTINLPTYTLEAVYEAI FGKPKEK VY A HEIAE AWE 300

Query: 301 SGENLERVAKYSMEDAKATYELGKEFLPMEIQLSRLV GQPLWDVRSSTGNLVEW FLLRK 360
        +G+ LERVAKYSMEDAK TYELG+EF PME QLSRLV GQPLWDVRSSTGNLVEW+LLRK
Sbjct: 301 TGKGLERVAKYSMEDAKVTYELGREFFPMEAQLSRLV GQPLWDVRSSTGNLVEW YLLRK 360

Query: 361 AYERNEVAPNKPSEEYQ RRLRESYTGGFVKEPEKGLWENIVYLDFRALPSIIITHN VS 420
        AYERNE+APNKP E EY+RRLRESY GG+VKEPEKGLWE +V LDFR+LYPSIIITHN VS
Sbjct: 361 AYERNELAPNKP DEREYERRLRESYAGGYVKEPEKGLWE GLVSLDFRSLYPSIIITHN VS 420

Query: 421 PDTLNLEGCKNYDIAPQVGHKFCKDIPGFIPSLLGHLLERQKIKTKMKETQDPIEKILL 480
        PDTLN EGC+ YD+AP+VGHKFCKD PGFIPSLL LL+ERQ+IK KMK ++DPIEK +L
Sbjct: 421 PDTLNREGCREYDV APEVGHKFCKD PFGFIPSLLKRL DDERQEIKRKMKA SKDPIEKKML 480

Query: 481 DYRQKAIKLLANS 493
        DYRQ+AIK+LANS
Sbjct: 481 DYRQRAIKILANS 493
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Figure 2--continued. Blast alignment of Pfu (query 1) against Deep Vent (subject 1)

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Score = 473 bits (1216), Expect = e-133
Identities = 248/283 (87%), Positives = 269/283 (94%)

Query: 492 NSFYGGYGYAKARWYCKECAESVTAWGRKYIELVWKELEEKFGFKVLYIDTDGLYATIPG 551
        NS+YGGYGYAKARWYCKECAESVTAWGR+YIE V KELEEKFGFKVLYIDTDGLYATIPG
Sbjct: 1029 NSYYGGYGYAKARWYCKECAESVTAWGREYIEFVRKELEEKFGFKVLYIDTDGLYATIPG 1088

Query: 552 GESEEIKKKALEFVKYINSKLPGLLELEYEGFYKRGFFVTKKRYAVIDEEGK VITRGLEI 611
        + EI IKKKALEFV YIN+KLPGLLELEYEGFY RGFFVTKK+YA+ IDEEGK+ITRGLEI
Sbjct: 1089 AKPEEIKKKALEFVDYINA KLPGLLELEYEGFYVRGFFVTKKYALIDEEGK IIITRGLEI 1148

Query: 612 VRRDWSEIAKETQARVLETILKHGDVEAVRIVKEVIQKLANYEIPPEKLA IYEQITRPL 671
        VRRDWSEIAKETQA+VLE ILKHG+VEEAV+IVKEV +KL+ YEIPPEKL IYEQITRPL
Sbjct: 1149 VRRDWSEIAKETQAKVLEAILKHGNVEEAVKIVKEVTEKLSKYEIPPEKL VIYEQITRPL 1208
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Query: 672 HEYKAIGPHVAVAKKLAAKGVKIKPGMVGIVYIVLRGDGPISNRAILAEELYDPKKHKYDAE 731  
HEYKAIGPHVAVAK+LAA+GVK++PGMVIGYIVLRGDGPIS RAILAEE+D +KHKYDAE  
Sbjct: 1209 HEYKAIGPHVAVAKRLAARGVKVRPGMVGIVYIVLRGDGPISKRAILAEFFDLRKHKYDAE 1268

Query: 732 YYIENQVLPALRILEFGYRKEDLRYQKTRQVGLTSWLNIKK 774  
YYIENQVLPALRILE FGYRKEDLR+QKT+Q GLT+WLNIKK  
Sbjct: 1269 YYIENQVLPALRILEAFGYRKEDLRWQTKQTGLTAWLNIKK 1311

**Figure 3. Assembly of the oligonucleotides into library fragments.**

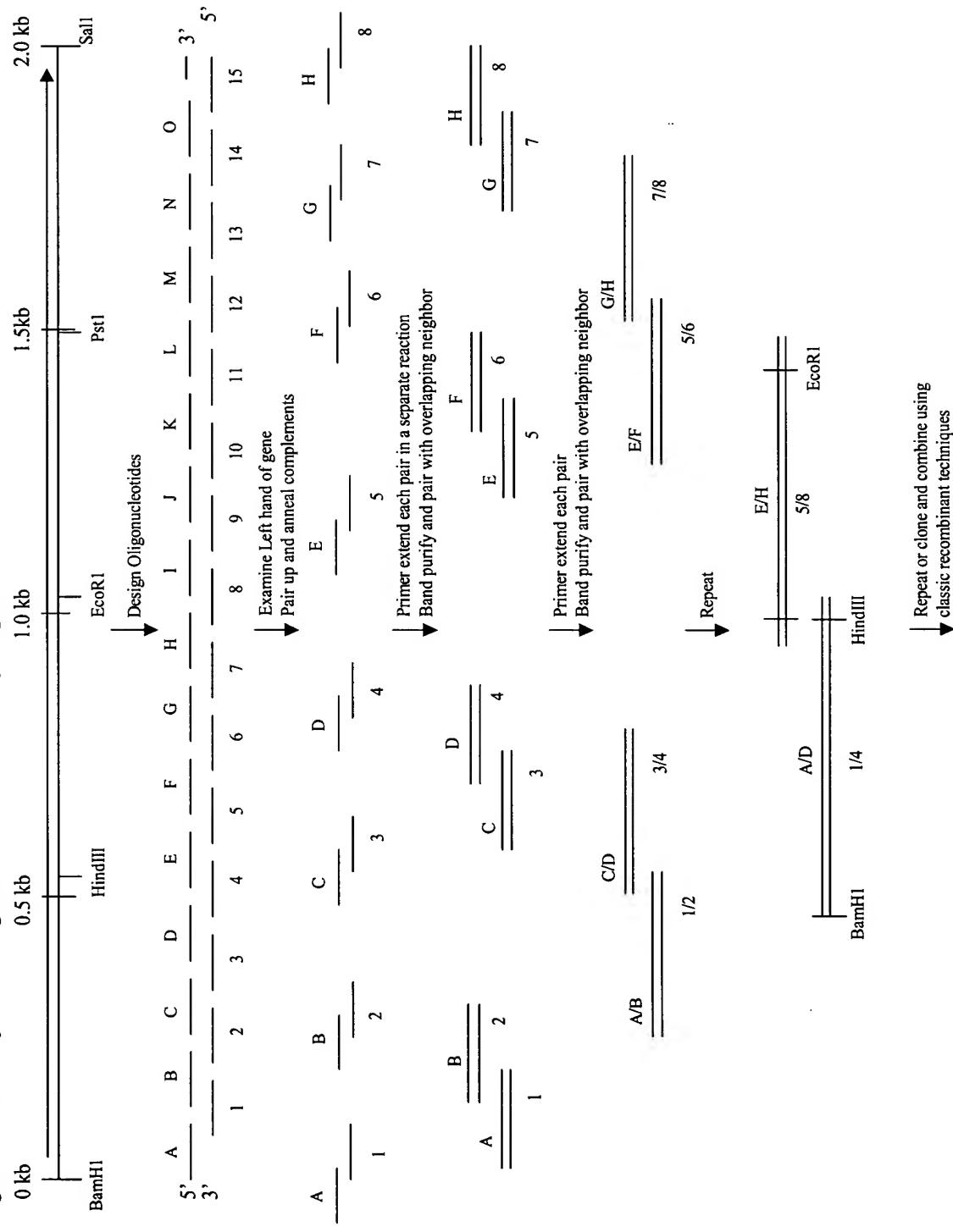


FIG. 4

E coli dut polypeptide sequence:

MKKIDVKILDPRVGKEFPLPTYATSGSAGLDLRACLNDAVELAPGDTTLVPTGLAIHIADPSLAAMMLPRSGLGHKG  
IVLGNLVGLIDSDYQGQLMISVWNRGQDSFTIQPGERIAQMIFVPVVQAEFNLVEDFDATDRGEGGFGHSGRQ

AAD polypeptide sequence:

MSKVILKIKRLPHAQDLPLPSYATPHSSGLDLRAAIEKPLKIKPFERVLIPTGLILEIPEGYEGQVRPRSGLAWKKGL  
TVLNAPGTIDADYRGEVKVILVNLGNEEVVIERGERIAQLVIAPVQRVEVVEEVSVTQRGEGGFGSTGTK

Alignment:

Identities = 61/149 (40%), Positives = 91/149 (60%), Gaps = 1/149 (0%)

Query: 1 MKKIDVKILDPRVGKEFPLPTYATSGSAGLDLRACLNDAVELAPGDTTLVPTGLAIHIAD 60  
M K+ +KI ++ PLP+YAT S+GLDLRA + +++ P + L+PTGL + I +  
Sbjct: 1 MSKVILKIKRLPHAQDLPLPSYATPHSSGLDLRAAIEKPLKIKPFERVLIPTGLILEIPE 60

Query: 61 PSLAAMMLPRSGLGHKGIVLGNLVGLIDSDYQGQLMISVWNRGQDSFTIQPGERIAQMI 120  
+ PRSGL K G+ + N G ID+DY+G++ + + N G + I+ GERIAQ++  
Sbjct: 61 -GYEGQVRPRSGLAWKKGLTVLNAPGTIDADYRGEVKVILVNLGNEEVVIERGERIAQLV 119

Query: 121 FVPVVQAEFNLVEDFDATDRGEGGFGHSG 149  
PV + E VE+ T RGEGGFG +G  
Sbjct: 120 IAPVQRVEVVEEVSVTQRGEGGFGSTG 148

**FIGURE 5**  
5A. Aligned parental sequence showing all possible codons

## 5B. The minimal encoding sequence

5C. A minimal encoding sequence after the removal of non-similar degeneracies; selection of ADD parent residues at particular sites

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## 5A. --continued

5B--continued

Min. Seq. GAT CTG CGT GCG TGC CTT AAC GAT GCG GTG GAA CTT GCG CCG GGT GAT ACG ACG CTG GTT CCG ACC GCC ATT CAT ATT GCG GAT CCT AT C G A C A GG

5C--continued

GAT	CTG	CGT	GCG	TGC	CTT	AAC	AAT	GCG	GTG	GAA	CTT	GCG	CCG	GGT	GAT	ACG	ACG	CTG	GTG	ATC	ATT	CAT	ATT	GCG	GAT	GGT					
GC	A	G	G	A	C	A	A	C	A	A	AA	TT	A	G	GT	A	G	TT	A	G	CCG	ACC	GGC	CTG	ATC	ATT	CAT	ATT	GCG	GAT	GGT
D	L	R	A	C	L	N	D	A	V	E	L	A	P	D	T	T	L	V	P	T	G	L	I	I	H	I	A	D	G		
D	S	K	A	I	E	K	P	L	K	I	K	F	E	R	V	I	L	E	V	M	D	A	C	T	G	P	E	O			

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5A--continued

5B--continued

Min.	TCT	CTG	GCG	ATG	ATG	CTG	CCG	CGT	AGC	GGC	CAT	AAA	CAT	GGC	ATA	GTG	CTG	GGG	AAC	CTG	GTG	ATT	GAT	AGC	GAT	TAT				
A ---	A	G	CA	G	G					C	TGG	A	G	T	AC	G	CT	GC	CC	AC	GC									
S	L	A	A	M	M	I	P	R	S	G	L	G	H	K	H	G	I	V	L	G	N	L	V	G	L	I	D	S	D	Y
Y	-	E	G	Q	V	R					A	W	K	L	T	V	L	A	P	T	A	P	A	V	P	A	T	A	M	

55 - continued

TCT	---	GCG	GCG	CAG	ATG	CTG	CCG	CGT	AGC	GGC	CTG	GGC	TGG	AAA	CAT	GGC	ATA	GTG	CTG	AAC	GGG	GTG	GGC	CTG	ATT	GAT	AGC	TAT	
A	A	G	G	G	G	G	C	C	A	G	T	A	G	C	A	G	T	A	C	G	CC	AC	AC	GC	GC				
S	-	A	A	Q	M	L	P	R	S	G	L	G	W	K	H	G	I	V	L	N	A	V	G	L	I	D	S	D	Y
Y		E	G	V	R							A		K		L	T	V			Q	A	P	T	A	P	T	T	M

5A--continued

5B--continued

Min.	Seq.	CAG	GGC	CAA	CTG	ATG	ATT	AGC	GTG	TGG	AAC	CGG	GGC	GAA	CGT	ATT	CAG	CCG	GGC	ATT	GCG	CAG	ATG	ATT	TTT	GTG	CCG				
G	G	G	G	A	G	T	C	GT	T	A	C	A	GA	G	GT	G	G	G	C	G	A	C	C	G	A	C					
Q	G	Q	L	M	I	S	V	W	N	R	G	Q	D	S	F	T	I	Q	P	G	E	R	I	A	Q	M	I	F	V	P	
R	E	V	K	V	I	L	N	L	N	L	N	E	E	E	V	V	E	R	V	V	E	R	I	A	Q	L	V	I	A	*	N

5C--continued

CAG	GGC	CAA	CTG	ATG	ATT	AGC	GTG	GTG	AAC	CGG	GGC	CAG	GAT	GAA	TTT	ACG	ATT	CAG	CCG	GAA	CGT	ATT	GGC	CAG	ATG	ATT	TTT	GTG	CCG	
G	G	G	A	G	T	C	T	A	C	A	G	GT	G	G	C	G	A	C	C	G	A	C	C	G	A	C	C	V	P	
Q	G	Q	L	M	I	S	V	N	N	R	G	Q	D	E	F	T	I	O	P	G	E	R	I	A	Q	M	I	F	V	P
R	E	V	K	V	I	L	L	N	E	V	V	E	R	N	M	H	H	M	L	V	I	A	L	V	I	A	K	A	K	

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5A--continued

5B--continued

5C--continued

FIGURE 6

**KpnI HindIII NdeI**

1 TT GGTAC<sub>C</sub> AAGCTT CAT ATG A(A/G) (A/C) AAA (A/G) TT (G/A) (A/T) T (G/C) TG AAA 38  
 AA CCATGG TTCGAA GTA TAC T(T/C) (T/G) TTT (T/C) AA (C/T) (T/A) A (C/G) AC TTT  
 M K/S/R/N K I/V D/I/V/N V/L K

39 ATT (C/A) (T/A) G CGT C(C/T) G C(G/C) T CAT G(G/C) C (A/C) AA GA(A/T) TT(T/A) 69  
 TAA (G/T) (A/T) C GCA G(G/A) C G(C/G) A GTA C(C/G) G (T/G) TT CT(T/A) AA(A/T)  
 I L/K/Q/M R P/L R/P H G/A K/Q E/D F/L

**StuI**

70 CCG CTG CCG A(C/G) C TAT GCG ACC (T/C) CT CAC AGC (G/T) CA GGC CTG GAT CTG 113  
 GGC GAC GGC T(G/C) G ATA CGC TGG (A/G) GA GTG TCG (C/A) GT CCG GAC CTA GAC  
 P L P T/S Y A T S/P H S A/S G L D L

114 CGT GCG (T/G) (G/C) C (C/A) TT (A/G) A(C/G) (A/G) A(T/A) (G/C) CG (G/C) TG (G/A) AA 140  
 GCA CGC (A/C) (C/G) G (G/T) AA (T/C) T(G/C) (T/G) T(A/T) (C/G) GC (C/G) AC (C/T) TT  
 R A C/A/S/G L/I N/E/K/D D/K/N/E A/P V/L E/K

141 (C/A) TT (G/A) (C/A) G CCG (G/T) (G/T) T GA(T/A) A(C/G) G (A/G) (C/T) G CTG 164  
 (G/T) AA (C/T) (G/T) C GGC (C/A) (C/A) A CT(A/T) T(G/C) C (T/C) (G/A) C GAC  
 L/I A/K/E/T P G/F/V/C D/E T/R T/V/M/A L

**AgeI**

165 (G/A) TT CCG ACC GGT CTG ATC (A/C) TT (C/G) A(T/A) ATT (G/C) CG GA(T/A) GGT 200  
 (C/T) AA GGC TGG CCA GAC TAG (T/G) AA (G/C) T(A/T) TAA (C/G) GC CT(A/T) CCA  
 V/I P T G L I I/L H/E/D/Q I A/P D/E G

201 T(C/A) T G(C/A) G G(C/G) G CAG (A/G) TG C(T/G) G CCG CGT AGC GGC CTG G(G/C) C 236  
 A(G/T) A C(G/T) C C(G/C) C GTC (T/C) AC G(A/C) C GGC GCA TCG CCG GAC C(C/G) G  
 S/Y A/E A/G Q M/V L/R P R S G L G/A

237 TGG AAA (C/A) A(T/G) GGC (A/T) TA (G/A) (T/C) G (C/G) TG CTG AAC GCG 266  
 ACC TTT (G/T) T(A/C) CCG (T/A) AT (C/T) (A/G) C (G/C) AC GAC TTG CGC  
 W K H/K/Q/N G I/L V/T/A/M L/V L N A

**ClaI**

267 (G/C) (T/C) G GGC (C/A) (T/C) G ATC GAT (A/G) (G/C) C GAT TAT C(A/G) G GGC 296  
 (C/G) (A/G) C CCG (G/T) (A/G) C TAG CTA (T/C) (C/G) G CTA ATA G(T/C) C CCG  
 V/P/A/L G L/T/P/M I D S/A/T/G D Y Q/R G

297 (C/G) AA (C/G) TG A(T/A) G (A/G) TT A(G/T) C (G/C) TG GTG AAC C(G/T) G GGC 326  
 (G/C) TT (G/C) AC T(A/T) C (T/C) AA T(C/A) G (C/G) AC CAC TTG G(C/A) C CCG  
 Q/E L/V M/K I/V S/I V/L N N R/L G

327 (C/A) A(G/C) GA(T/A) GAA (T/G) TT (A/G) (C/T) G ATT (C/G) AG C(C/G) G GGC GAA 356  
 (G/T) T(C/G) CT(A/T) CTT (A/C) AA (T/C) (G/A) C TAA (G/C) TC G(G/C) C CCG CTT  
 Q/N/H/K D/E E F/V T/V/M/A I Q/E P/R G E

**FspI**

357 CGT ATT GCG CAG (A/C) TG (A/G) TT (T/A) TT G(T/C) G CCG GTG (G/C) (T/A) G 389  
 GCA TAA CGC GTC (T/G) AC (T/C) AA (A/T) AA C(A/G) C GGC CAC (C/G) (A/T) C  
 R I A Q M/L I/V F/I V/A P V V/Q/E/L

390 C(A/G) G G(C/T) G GAA (T/G) TT (A/G) (A/T) T (C/G) (T/A) G GTG GAA GA(T/A) 416  
 G(T/C) C C(G/A) C CTT (A/C) AA (T/C) (T/A) A (G/C) (A/T) C CAC CTT CT(A/T)  
 Q/R A/V E F/V N/V/I/D L/E/Q/V V E D/E

417 (T/G) TT TCT CAG ACC (G/C) A(T/G) CGT GGC GAA GGC GGC TTT GGC TCT A(G/C) C 458  
 (A/C) AA AGA GTC TGG (C/G) T(A/C) GCA CCG CTT CCG CCG AAA CCG AGA T(C/G) G  
 F/V S Q T D/Q/E/H R G E G G F G S S/T

**BamHI EcoRI**

459 GGC A(G/C) A (C/A) AG TAA TGA GGATCC GAATTC TT 487  
 CCG T(C/G) T (G/T) TC ATT ACT CCTAGG CTTAAG AA  
 G R/T Q/K \* \*

Figure 7

10            20            30            40            50            60            70  
TTGGTACCAAGCTTCATATGARMAARTTRWTSTGAAAATTMWCGCTCYGCSTCATGSCMAAGAWTTWCC  
AACCATGGTTCGAAGTATACTYKTTTYAAYWASACTTTAAKWCAGRCGSAGTACSGKTTCTWAAGGG  
  
80            90            100          110          120          130          140  
GCTGCCGASCTATGCACCCYCTCACAGCKCAGGCCCTGGATCTGCGTGCCKSCMTTRASRAWSCGSTGRAA  
CGACGGCTSGATAACGCTGGRGAGTGTCGMGTCCGGACCTAGACGCACGCMMSGKAAYTSYTWSGCSACYTT  
  
150          160          170          180          190          200          210  
MTTRMGCGKKTGAWASGRYGCCTGRTTCCGACCGGTCTGATCMTTSAWATTSCGGAWGGTTMTGMGGSGC  
KAAVKCGGCMMACTWTSCYRCGACYAAGGCTGCCAGACTAGKAASWTAAAGCCTWCCAACKCCSCG  
  
220          230          240          250          260          270          280  
AGRTGCKGCCGCGTAGCGGCCTGGCTGGAAAMAKGGCWTARYGSTGCTGAACGCCSYGGGCMYGATCGA  
TCYACGMCGGCGCATGCCGGACCSGACCTTAKMCCGWATYRCSACGACTTGCGCSRCCGKRCTAGCT  
  
290          300          310          320          330          340          350  
TRSCGATTATCRGGGCSASTGAWGRTTAKCSTGGTGAACCKGGGCMASGAAKTRYGATTSAGCSG  
AYSGCTAATAGYCCCGSTSACTWCYAATMGSACCAC TTGGMCCGKTSCTWCTTMAAYRCTAASTCGSC  
  
360          370          380          390          400          410          420  
GGCGAACGTATTGCGCAGMTGRTTWTGYGCCGGTGSWGRGGYGGAAKTRYGATTCGAATTCTT  
CCGCTTGATAACCGTCKACYAAWAACRCGGCCACSWCGYCCRCCTTMAAYWASWCCACCTCTWMAAA  
  
430          440          450          460          470          480  
CTCAGACCSAKCGTGGCGAAGGCGGCTTGGCTCTASCGGCASAMAGTAATGAGGATCCGAATTCTT  
GAGTCTGGSTMGCACCGCTTCCGCCAAACCGAGATSGCCGTTKCATTACTCCTAGGCTTAAGAA

Figure 8.

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atg atc ctg gat g(t/c)t gac tac atc act gaa ga(a/c) ggc aaa ccg (g/a)tt atc cgt (c/a)t(g/c) ttc  
M I L D V/A D Y I T E E/D G K P V/I I R L/I/M F  
  
aaa aaa gag aac ggc (a/g)aa ttt aag (a/g)tt gag (c/t)at gat cgc a(a/c)c ttt cgt cca tac att tac gct  
K K E N G K/E F K I/V E H/Y D R N/T F R P Y I Y A  
  
ctg ctg a(g/a)a gat gat tct (a/c)ag att ga(g/t) gaa gtt a(g/a)a aaa atc act g(g/c)t gag cgc cat ggc aag att  
L L R/K D D S K/Q I E/D E V K/R K I T G/A E R H G  
K I

214 215

gtt cgt atc (a/g)tt gat g(t/c)g gaa aag gta (g/a)(g/a)g aag aaa ttt ctg ggc a(a/g)a cca atc (a/g)(a/c)g  
V R I I/V D V/A E K V G/E/R/K K K F L G K/R P I  
K/T/E/A  
  
gtg tgg a(g/a)a ctg tat (c/t)tc gaa cat cca caa gat gtt ccg a(t/c)t att cgc ga(g/t) aaa (g/a)tt cgc  
V W K/R L Y L/F E H P Q D V P T/A I R E/D K V/I R  
  
gaa cat (c/t)ct gca gtt (g/a)tt gac atc ttc gaa tac gat att cca ttt gca aag cgt tac ctc atc gac aaa  
E H P/S A V V/I D I F E Y D I P F A K R Y L I D K  
  
ggc ctg ata cca atg gag ggc ga(g/t) gaa gaa ctc aag (a/c)tc ctg gcg ttc gat ata gaa acc ctc tat  
G L I P M E G E/D E E L K I/L L A F D I E T L Y  
  
cac gaa ggc gaa gag ttt g(g/c)t aaa ggc cca att ata atg att agc tat gca gat gaa (a/g)a(a/c) gaa gca aag  
H E G E E F G/A K G P I I M I S Y A D E K/N/E/D E A  
K  
  
gtg att act tgg aaa aa(a/c) ata gat ctc cca tac gtt gag gtt gta tct tcc gag cgc gag atg att aag cgc  
V I T W K K/N I D L P Y V E V V S S E R E M I K R  
  
ttt ctc a(g/a)a (g/a)tt atc cgc gag aag gat ccg gac (g/a)tt atc (g/a)tt act tat aac ggc gac tct ttt  
F L R/k V/I I R E K D P D V/I I V/I T Y N G D S F  
  
gac (c/t)tc cca tat ctg g(t/c)g aaa cgc gca gaa aaa ctc ggt att aaa ctg (a/c)ct (a/c)tc ggc cgt gat ggt  
D F P Y L V/A K R A E K L G I K L T/P I/L G R D  
G  
  
tcc gag ccg aag atg cag cgt (a/c)tc ggc gat atg acc gct gta gaa (g/a)tt aag ggt cgt atc cat ttc gac  
S E P K M Q R I/L G D M T A V E V/I K G R I H F D  
  
ctg tat cat gta att (a/c)(c/g)c cgt act att aac ctc ccg act tac act ctc gag gct gta tat gaa gca att  
L Y H V I T/S/P/R R T I N L P T Y T L E A V Y E A I  
  
ttt ggt aag ccg aag gag aag gta tac gcc (g/c)at gag att gca (a/g)ag ggc tgg gaa (a/t)cc ggt (a/g)ag  
F G K P K E K V Y A D/H E I A K/B A W E T/S G K/E  
  
(a/g)(a/g)c ctc gag cgt gtt gca aaa tac tcc atg gaa gat gca aag g(t/c)g act tat gaa ctc ggc a(g/a)a gaa ttc  
N/G/D/S L E R V A K Y S M E D A K V/A T Y E L G R/K  
E F

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(c/t)tc cca atg gaa (a/g)(t/c)t cag ctc tct cgc ctg gtt ggc caa cca ctg tgg gat gtt tct cgt tct tcc  
L/F P M E I/T/V/A Q L S R L V G Q P L W D V S R S S

acc ggt aac ctc gta gag tgg t(t/a)t ctc ctg cgc aaa gcg tac gaa cgc aac gaa (g/c)tg gct ccg aac aag  
T G N L V E W F/Y L L R K A Y E R N E V/L A P N K

cca (t/g)(c/a)c gaa (c/g)(g/a)a gag tat (c/g)aa cgc cgt ctc cgc gag tct tac (a/g)ct ggt ggc t(t/a)t  
P S/Y/A/D E R/Q/G/E E Y Q/E R R L R E S Y T/A G G F/Y

gtt aaa gag cca gaa aag ggc ctc tgg gaa (a/g)(a/g)c (a/c)tc gtg t(c/a)c ctc gat ttt cgc (g/t)ct ctg  
V K E P E K G L W E N/S/D/G I/L V Y/S L D F R A/S L

tat ccg tct att atc att acc cac aac gtg tct ccg gat act ctc aac c(t/g)c gag ggc tgc a(g/a)a  
Y P S I I T H N V S P D T L N L/R E G C K/R

(a/g)a(a/c) tat gat (g/a)tt gct ccg (c/g)aa gta ggc cac aag ttc tgc aag gac (a/t)tc ccg ggc ttt att  
K/N/E/D Y D V/I A P Q/E V G H K F C K D I/F P G F I

ccg tct ctc ctg (a/g)(a/g)g c(a/g)t ctg ctc ga(g/t) gaa cgc caa (a/g)ag att aag (a/c)(g/c)c aaa atg aag  
P S L L K/R/E/G R/H L L E/D E R Q K/E I K T/S/P/R K M K

g(a/c)g (a/t)cc (c/a)ag gat ccg att gaa aaa a(t/a)a (a/c)tg ctc gac tat cgc caa a(g/a)a gcg att aaa  
E/A T/S Q/K D P I E K I/K M/L L D Y R Q R/K A I K

(a/c)tc ctc gca aac tct t(a/t)t tac ggc tat tat ggc tat gca aaa gca cgc tgg tac tgt aag gag tgt gct  
L/I L A N S F/Y Y G Y G Y A K A R W Y C K E C A

gag tcc gtt act gct tgg ggt cgc (a/g)aa tac atc gag (c/t)tc gtg (t/c)gg aag gag ctc gaa gaa aag ttt ggc  
E S V T A W G R K/E Y I E L/F V W/R K E L E E K F G

ttt aaa gtt ctc tac att gac act gat ggt ctc tat gcg act att ccg ggt g(g/c)t (a/g)ag (c/t)ct gag  
F K V L Y I D T D G L Y A T I P G G/A E/K S/P E

1696

gaa att aag aaa aag gct ctc gaa ttt gtg **aaa** tac att aac (g/t)cg aag ctc ccg ggt ctc ctg gag ctc gaa  
E I K K A L E F V K(D) Y I N A/S K L P G L L E L E

tat gaa ggc ttt tat (g/a)(t/a)g cgc ggc ttc ttc gtt acc aag aag a(g/a)a tat gcg (g/c)tg att gat gaa gaa  
Y E G F Y V/E/M/K R G F V T K K R/K Y A V/L I D E E

ggc aaa (g/a)tt att act cgt ggt ctc gag att gtg cgc cgt gat tgg agc gaa att gcg aaa gaa act caa gct  
G K V/I I T R G L E I V R R D W S E I A K E T Q A

a(g/a)a gtt ctc gag (a/g)ct att ctc aaa cac ggc (g/a)ac gtt gaa gaa gct gtg a(g/a)a att gta aaa gaa gta  
R/K V L E T/A I L K H G D/N V E E A V R/K I V K E V

a(t/c)c (c/g)aa aag ctc (g/t)ct aa(a/c) tat gaa att ccg cca gag aag ctc g(t/c)g att tat gag cag att  
I/T Q/E K L A/S K/N Y E I P P E K L V/A I Y E Q I

act cgc ccg ctg cat gag tat aag gcg att ggt ccg cac gtg gct gta aag a(g/a)a ctg gct gct a(g/a)a ggc gtg  
T R P L H E Y K A I G P H V A V A K R/K L A A K/R G V

aaa (g/a)tt a(g/a)a ccg ggt atg gta att ggc tac att gta ctc cgc ggc gat ggt ccg att agc aa(a/c) cgt gca  
K V/I R/K P G M V I G Y I V L R G D G P I S K/N R A

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att cta gct gag gaa t(t/a)c gat c(c/t)g a(g/a)a aag cac aag tat gac gca gaa tat tac att gag aac cag gtg  
I L A E E F/Y D P/L K/R K H K Y D A E Y Y I E N Q V  
2272 2273

ctc ccg gcg gta ctc cgt att ctg gag g(g/c)t ttt ggc tac cgt aag gaa gac ctc cgc t(a/g)(c/g) caa aag  
L P A V L R I L E G/A F G Y R K E D L R Y/W/\*/C Q K

act a(g/a)a cag (g/a)(t/c)t ggc ctc act (g/t)ct tgg ctc aac att aaa aaa tcc ggt acc cac tag tgc tag cat gac  
T K/R Q V/A/I/T G L T A/S W L N I K K S G T H \*

Figure 9. A comparison of the polymerase to 3' to 5' exonuclease activity

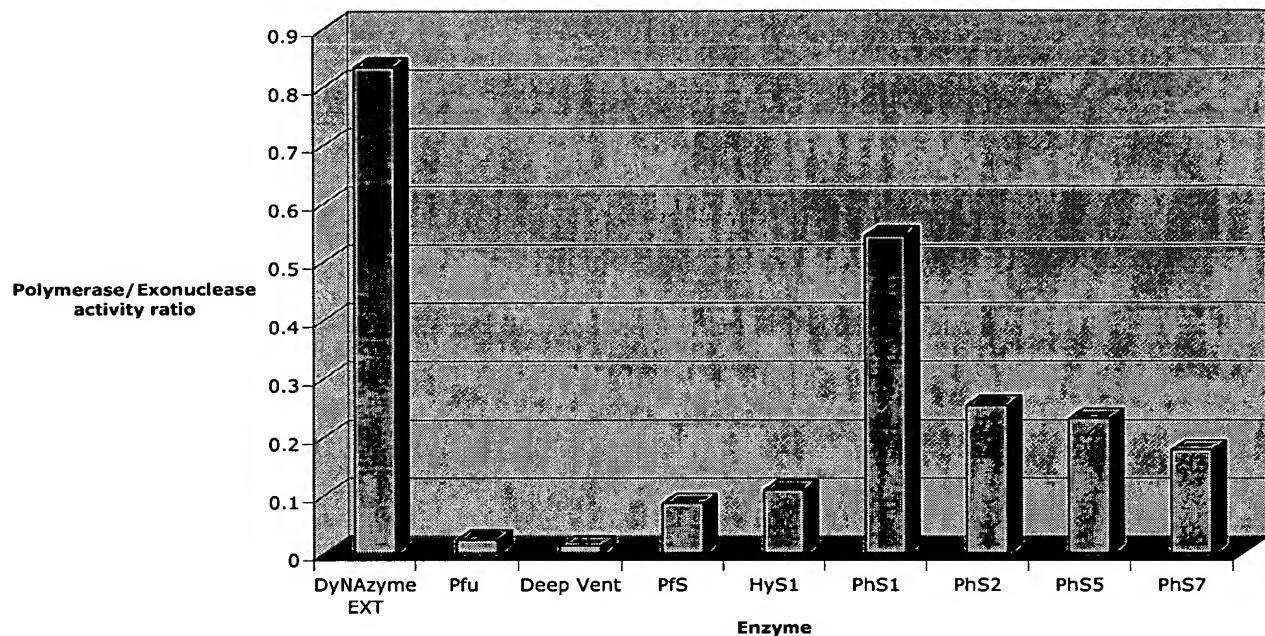


FIGURE 10

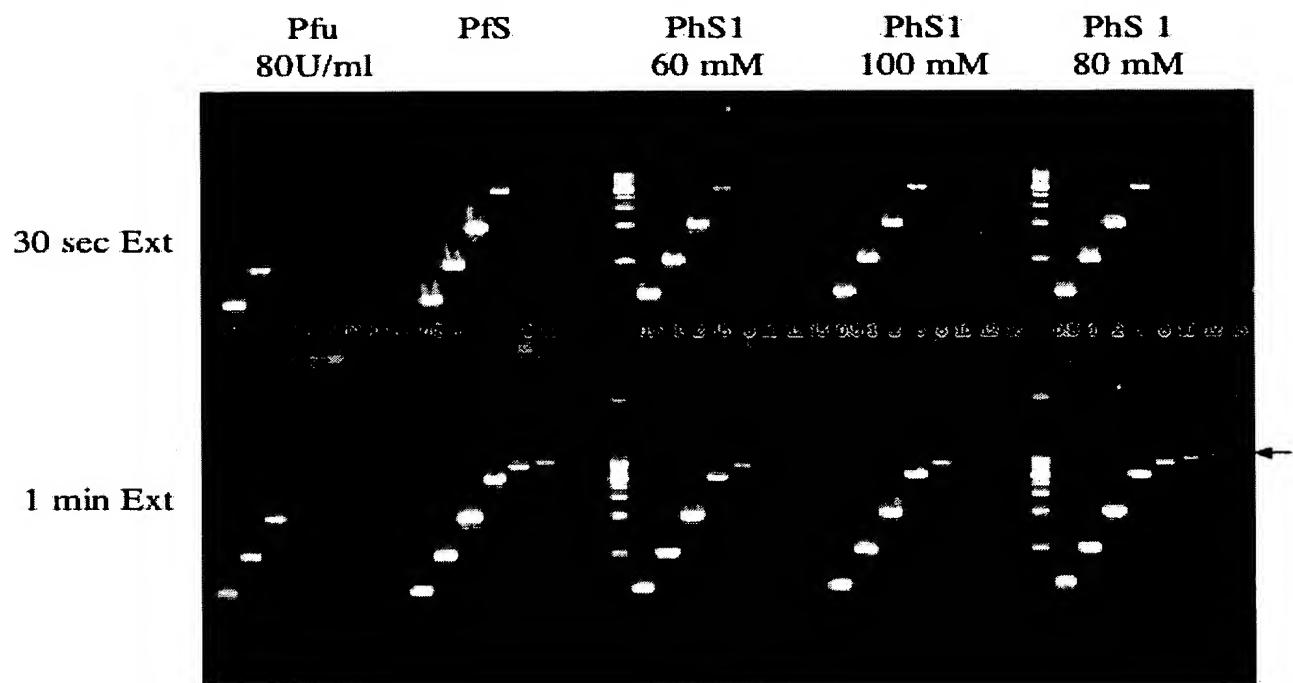


Figure 11

**Pfu**    **DeepVent**    **Hybrid\_design**

**Hybrid\_design** (highlighted in yellow)

**Hybrid\_design** (highlighted in red)

**Hybrid\_design** (highlighted in green)

**Hybrid\_design** (highlighted in blue)

**Hybrid\_design** (highlighted in purple)

**Hybrid\_design** (highlighted in orange)

**Hybrid\_design** (highlighted in pink)

**Hybrid\_design** (highlighted in grey)

**Hybrid\_design** (highlighted in black)

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Pfu	AYERNEVAPNPKPSLELYQKRLRESYTGCFVKPELKGLWENIVLDLFWALYPSIIITHNVS	370				
DeepVent	AYERNELAPNPKPDEEYERRRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS	380				
Hybrid_design	AYERNEVAPNPKPDXEYXERRRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS	390				
HyS1	AYERNEVAPNPKPDXEYXERRRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS	400				
Hyb2	AYERNELAPNPKPDXEYERRRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS	410				
Hyb3	AYERNELAPNPKPDXEYERRRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS	420				
HyS4	AYERNELAPNPKPDXEYERRRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS					
PhS1	AYERNELAPNPKPDXEYERRRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS					
PhS2	AYERNELAPNPKPDXEYERRRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS					
PhS3	AYERNELAPNPKPDXEYERRRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS					
PhS4	AYERNEVAPNPKPSLELYQKRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS					
PhS5	AYERNEVAPNPKPDXEYERRRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS					
PhS6	AYERNEVAPNPKPDXEYERRRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS					
PhS7	AYERNEVAPNPKPDXEYERRRLRESYAGGYVKEPEBKGLWENIVLDLFWALYPSIIITHNVS					
Pfu	PDTLNLLEGCKNYDIAPOVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKEHQDPFIEKIL	430				
DeepVent	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL	440				
Hybrid_design	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL	450				
HyS1	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL	460				
Hyb2	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL	470				
Hyb3	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL					
HyS4	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL					
PhS1	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL					
PhS2	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL					
PhS3	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL					
PhS4	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL					
PhS5	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL					
PhS6	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL					
PhS7	PDTLNLREGCKEYDVAPEVGHKFKCKDIPGFTPSLQLCGLLEFQKIKTKMKKAASKDPFIEKIL					
Pfu	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY	480				
DeepVent	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY	490				
Hybrid_design	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY	500				
HyS1	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY	510				
Hyb2	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY	520				
Hyb3	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY	530				
HyS4	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY	540				
PhS1	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY					
PhS2	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY					
PhS3	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY					
PhS4	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY					
PhS5	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY					
PhS6	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY					
PhS7	DYRQKAKIILANSYYGYYGYYAKARWYCKEGASVTAWGRREYIEFVWKELEEKFGFKVLY					
Pfu	DIDDGLYATIPCGESSEIIEKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	550				
DeepVent	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	560				
Hybrid_design	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	570				
HyS1	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	580				
Hyb2	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	590				
Hyb3	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	600				
HyS4	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	610				
PhS1	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
PhS2	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
PhS3	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
PhS4	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
PhS5	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
PhS6	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
PhS7	DIDDGLYATIPCGAKPEEIKKKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
Pfu	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	620				
DeepVent	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	630				
Hybrid_design	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	640				
HyS1	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	650				
Hyb2	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	660				
Hyb3	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	670				
HyS4	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE	680				
PhS1	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
PhS2	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
PhS3	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
PhS4	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
PhS5	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
PhS6	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
PhS7	DEGG - DVAIITIPCGAKSLEIIXKAKLEFVKYINSKLPGGLEELYEGFYKRGEFVTKKRYAVIDE					
Pfu	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE	690				
DeepVent	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE	700				
Hybrid_design	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE	710				
HyS1	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE	720				
Hyb2	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE	730				
Hyb3	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE	740				
HyS4	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE	750				
PhS1	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE					
PhS2	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE					
PhS3	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE					
PhS4	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE					
PhS5	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE					
PhS6	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE					
PhS7	LAIYEQIITRPLHEYKAIGCPHYAVAKRPLAARGCVKIKPGMVIGYIVLRLGCDGPISNRAILAE					

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Pfu	<u>YDPLKKHKYDAAEYYIENQVLPAVLRLILEGFCYRKEDLKVQLTRQVGLTSWLNIIKKK</u>	700	740	750	760	770	780
DeepVent	<u>FDLRKHKYDAAEYYIENQVLPAVLRLILEAPFCYRKEDLRWQTKQIGLTAWLNIIKKK</u>						
Hybrid_design	<u>DPKHKYDAAEYYIENQVLPAVLRLILEXPFCYRKEDLRWQRTKQXGLTXWLNIKKSGTHNC</u>						
HyS1	<u>DPKHKYDAAEYYIENQVLPAVLRLILEBFCYRKEDLRWQRTKQAGLTAWLNIIKKSGTCGG</u>						
Hyb2	<u>FDLRKHKYDAAEYYIENQVLPAVLRLILECFCYRKEDLRLRN</u>						
Hyb3	<u>FDPKHKYDAAEYYIENQVLPAVLRLILEBFCYRKEDLRLRN</u>						
Hyb4	<u>FDPKHKYDAAEYYIENQVLPAVLRLILEGFCYRKEDLRLRN</u>						
PhS1	<u>YDPLKKHKYDAAEYYIENQVLPAVLRLILEGFCYRKEDLRWQTKQAGLTAWLNIIKKSGTCGG</u>						
PhS2	<u>YDPLKKHKYDAAEYYIENQVLPAVLRLILEAPFCYRKEDLRYQTKQVGLTACLNIIKKSGTCGG</u>						
PhS3	<u>YDPLKKHKYDAAEYYIENQVLPAVLRLILEAPFCYRKEDLRYQTKQVGLTACLNIIKKSGTCGG</u>						
PhS4	<u>YDPLKKHKYDAAEYYIENQVLPAVLRLILEAPFCYRKEDLRWQTKQVGLTAWLNIIKKSGTCGG</u>						
PhS5	<u>YDPLKKHKYDAAEYYIENQVLPAVLRLILEAPFCYRKEDLRWQTKQVGLTAWLNIIKKSGTCGG</u>						
PhS6	<u>YDPLKKHKYDAAEYYIENQVLPAVLRLILEAPFCYRKEDLRWQTKQVGLTAWLNIIKKSGTCGG</u>						
PhS7	<u>YDPLKKHKYDAAEYYIENQVLPAVLRLILEAPFCYRKEDLRWQTKQVGLTAWLNIIKKSGTCGG</u>						

Pfu		700	740	750	760	770	780
DeepVent	NHD						
Hybrid_design	<u>GATVKFKYKGEEKEVDITSKIKVWKVVKMISFTYDEGGCKTGAVSEKDAPIKELQML</u>						
HyS1	<u>GATVKFKYKGEEKEVDISKIKVWKVVKMISFTYDEGGCKTGAVSEKDAPIKELQML</u>						
Hyb2	<u>GATVKFKYKGEEKEVDISKIKVWKVVKMISFTYDEGGCKTGAVSEKDAPIKELQML</u>						
Hyb3	<u>GATVKFKYKGEEKEVDISKIKVWKVVKMISFTYDEGGCKTGAVSEKDAPIKELQML</u>						
Hyb4	<u>GATVKFKYKGEEKEVDISKIKVWKVVKMISFTYDEGGCKTGAVSEKDAPIKELQML</u>						
PhS1	<u>GATVKFKYKGEEKEVDISKIKVWKVVKMISFTYDEGGCKTGAVSEKDAPIKELQML</u>						
PhS2	<u>GATVKFKYKGEEKEVDISKIKVWKVVKMISFTYDEGGCKTGAVSEKDAPIKELQML</u>						
PhS3	<u>GATVKFKYKGEEKEVDISKIKVWKVVKMISFTYDEGGCKTGAVSEKDAPIKELQML</u>						
PhS4	<u>GATVKFKYKGEEKEVDISKIKVWKVVKMISFTYDEGGCKTGAVSEKDAPIKELQML</u>						
PhS5	<u>GATVKFKYKGEEKEVDISKIKVWKVVKMISFTYDEGGCKTGAVSEKDAPIKELQML</u>						
PhS6	<u>GATVKFKYKGEEKEVDISKIKVWKVVKMISFTYDEGGCKTGAVSEKDAPIKELQML</u>						
PhS7	<u>GATVKFKYKGEEKEVDISKIKVWKVVKMISFTYDEGGCKTGAVSEKDAPIKELQML</u>						

Pfu		650	660	670	680	690	700
DeepVent							
Hybrid_design	<u>KQKKN</u>						
HyS1	<u>KQKKN</u>						
Hyb2	<u>KQKKN</u>						
Hyb3	<u>KQKKN</u>						
Hyb4	<u>KQKKN</u>						
PhS1	<u>KOKKN</u>						
PhS2	<u>KOKKN</u>						
PhS3	<u>KOKKN</u>						
PhS4	<u>KOKKN</u>						
PhS5	<u>KOKKN</u>						
PhS6	<u>KOKKN</u>						
PhS7	<u>KOKSK</u>						